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EXAMINER	
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ART UNIT	PAPER NUMBER
1654	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/567,406	LANGE ET AL.	
	Examiner	Art Unit	
	Julie Ha	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 August 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5,6,13-20,22,23,27-29,31,33-35,37,39,40,43 and 44* is/are pending in the application.

4a) Of the above claim(s) *5* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,6,13-20,22,23,27-29,31,33-35,37,39,40,43 and 44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Election/Restriction filed on August 23, 2007 is acknowledged. Claims 1-3, 5, 6, 13-20, 22-23, 27-29, 31, 33-35, 37, 39, 40, 43 and 44 are pending in this application.

Restriction

1. Applicant's election with traverse of Group I (claims 1-3, 5-6, 13-20, 22-23, 27-29, 31, 37, 39-40 and 43-44), drawn to a method for prophylaxis or treatment of cancer cachexia in an individual in need thereof comprising administration to said individual of a ghrelin-like compound or a pharmaceutically acceptable salt thereof and election of SEQ ID NO:1 for species election, in the reply filed on August 23, 2007 is acknowledged. The traversal is on the ground(s) that wild-type ghrelin is a 28-amino peptide with a modified internal serine, and Bednarek reference cited by the Examiner teaches a truncated ghrelin "having the structure Z^1-GSXF$(Z)_n$-Z^2 or Z^1-GXSF$(Z)_n$-Z^2", wherein n is 0-19. Since Bednarek teaches that the invention is directed to truncated ghrelin analogues, and that their smaller size is advantageous, it follows that Bednarek's formula should not be construed as reading on ghrelin analogues as long as, or longer than, wild-type ghrelin. Therefore, Bednarek's "has" must be interpreted as a "closed" term. Furthermore, Applicant argues that SEQ ID NO:1 consists of 28 amino acids, an analogue under (b) must consist of at least 26 amino acids, since 28*0.9= 25.2. Furthermore, Applicant argues that Bednarek does not teach the combination of administration of a ghrelin-like compound with an anti-neoplastic treatment, in order to

prevent or treat cancer. Additionally, Applicant argues that the species are not mutually exclusive. It is clear that "at least 80% includes, as a subset "at least 90%", and "at least 90%" includes "at least 98%". This is not found persuasive because claim 1 recites the ghrelin-like compound comprises a structure defined by formula I Z^1-$(X^1)_m$-(X^2)-$(X^3)_n$-Z^2, wherein Z^1 is an optionally present protecting group, each X^1 is independently selected from an amino acid, X^2 is any amino acid selected form the group consisting of naturally occurring and synthetic amino acids, the amino acid being modified with a bulky hydrophobic group, each X^3 is independently selected from an amino acid, wherein the amino acid is selected from the group consisting of naturally occurring and synthetic amino acids, wherein one or more of X^1 and X^3 optionally may be modified with a bulky hydrophobic group, Z^2 is an optionally present protecting group, m is an integer in the range of from 1-10, n is 0 or an integer in the range of from 1-35, and wherein (a) the ghrelin-like compound or pharmaceutically acceptable salt thereof is 27-28 amino acids in length, with the proviso that the ghrelin-like compound is at least 80% homologues to SEQ ID NO:1, such as at least 85 % homologues to SEQ ID NO:1 and/or (b) the ghrelin-like compound is at least 90% homologous to SEQ ID NO: 1. As indicated by previous office action, Bednarek patent 6967237 teaches SEQ ID NO:1 wherein Ser at 3rd position is modified with a bulky hydrophobic R group (see column 2, lines 55-64) having the structure Z^1-GSXF$(Z)_n$-Z^2 or Z^1-GXSF$(Z)_n$-Z^2 wherein Z^1 is an optionally present protecting group and Z^2 is an optionally present protecting group, and n is 0 to 19 (see column 3, lines 17). Since instant claim 1 recites (a) and/or (b), this implies that the ghrelin-like compound may be 80% of 27-28 amino acids in length and/or 90% of

27-28 amino acids in lengths. Bednarek patent teaches SEQ ID NO:4 that has 23 amino acids in lengths. 80% of 27 amino acids = 21.6, thus 22 amino acids in lengths, and 80% of 28 amino acids = 22.4, thus 23 amino acids in lengths. Since the Applicant argues that "at least 80% includes at least 90% and at least 90% includes at least 98%" (see Applicant's Election with Traverse on p. 3), this implies that Bednarek's SEQ ID NO:4 meets the limitation of all of the claimed homologs (i.e., at least 80%, at least 90%, at least 98%). Therefore, Bednarek patent teaches all of the limitations of instant claim 1. Contrary to Applicant's arguments, at least 90% implies that there are 2 amino acids that are different from the wild-type sequence. This means that there are 28*2=56 different possible sequence variances. Furthermore, Bednarek patent does not teach that the ghrelin-like compound is in the "closed" form as the Applicant argues. As indicated by SEQ ID NOS: 1-21, the sequences do not end in amide at the N- or carboxyl at the C-terminal ends of the sequence. Therefore the unity of the invention is broken. Additionally, the Group restriction is divided into treating cancer cachexia (Group I) and cancer (Group II), therefore, since Bednarek patent teaches treating cancer cachexia (Group I), the unity of invention is further broken. However, due to Applicant's amendment to claims 33-35, these claims have been rejoined with Group I.

2. The requirement is still deemed proper and is therefore made FINAL. Claim 5 is withdrawn from further consideration, as being drawn to nonelected species. Claims 1-3, 6, 13-20, 22-23, 27-29, 31, 33-35, 37, 39, 40, 43-44 are examined on the merits in this office action.

Objection-Minor Informalities

3. The title is objected to because the title is too long. The title is limited to 2-7 words maximum. A new title is required that is clearly indicative of the invention to which the claims are directed.

4. Claim 1 is objected to because the claim language seems too "wordy". At line 2, the claim recites, "treatment of cancer cachexia in an individual in need of thereof". The phrase "in need of thereof" seems "wordy" and should be changed to "in need thereof". At line 3, the claim recites, " comprising administration to said individual of a ghrelin-like". The word "of" seems too "wordy" and should be deleted.

Rejection-35 U.S.C. 112, 2nd

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required

feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claims 1 and 39 recite the broad recitation "(a)...27-28 amino aids in length, with the proviso that said ghrelin-like compound is at least 80% homologous to SEQ ID NO:1", and the claim also recites "such as at least 85% homologous to SEQ ID NO:1 and/or at least 90% homologous to SEQ ID NO: 1" which is the narrower statement of the range/limitation.

7. Regarding claims 1 and 39, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

8. Claims 1 and 39 also recite the formula Z^1-$(X^1)_m$-(X^2)-$(X^3)_n$-Z^2 and the limitation wherein m is an integer in the range of from 1-10, n is 0 or an integer in the range of from 1-35, and wherein (a) the ghrelin-like compound or pharmaceutically acceptable salt thereof is 27-28 amino acids in length. It is unclear how a ghrelin-like compound of 27-28 amino acids in length is possible if m is 10 and n is 0. This would only lead to a compound that is 11 amino acids in lengths. This would not be at least 80% homologous to SEQ ID NO: 1 (28*0.8=23 amino acids).

Rejection-35 U.S.C. 112, 1st

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1-2, 6, 14-20, 22-23, 27-29, 31, 33-35, 37, 39, 40 and 43-44 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

> "To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966." Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

11. The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." MPEP 2163.

12. Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In Regents of the University of California v. Eli Lilly & Co., the court stated:

"A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials. Fiers, 984 F.2d at 1171, 25 USPQ2d at 1606; In re Smythe, 480 F.2d 1376, 1383, 178 USPQ 279, 284-85 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus. . . ."). Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

13. The MPEP further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP 2163. The MPEP does state that for generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP 2163. Although the MPEP does not define what constitute a sufficient number of representative, the Courts have indicated what do not constitute a representative number species to adequately describe a broad generic. In Gostelli, the Court determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872 F.2d at 1012, 10 USPQ2d at 1618.

14. In the instant case, the claims are drawn to a method for prophylaxis or treatment of cancer cachexia and a method for stimulation of appetite in an individual in need thereof, comprising administration to said individual a ghrelin-like compound or a pharmaceutically acceptable salt thereof, wherein said ghrelin-like compound or pharmaceutically acceptable salt thereof is 27-28 amino acids in lengths, with the proviso that said ghrelin-like compound is at least 80% homologous to SEQ ID NO: 1, at

least 85 % homologous to SEQ ID NO: 1, at least 90% homologous to SEQ ID NO:1. The generic statements ghrelin-like compounds and 27-28 amino acids in lengths, with the proviso that the ghrelin-like compound is at least 80% homologous to SEQ ID NO:1, at least 85 % homologous to SEQ ID NO:1, at least 90% homologous to SEQ ID NO: 1 and at least 95% homologous to SEQ ID NO:1 do not provide ample written description for the compounds since the claims do not describe a single structural feature. The specification does not clearly define or provide examples of what qualify as compounds of the claimed invention.

15. As stated earlier, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. It is unquestionable claims 1 and 39 are broad generics with respect all possible compounds encompassed by the claims. The possible structural variations are limitless to any class of peptide or a peptide-like molecule that can form peptide bonds and make up the ghrelin like compounds (such as antagonists, agonists, variants and homologs). It must not be forgotten that the MPEP states that if a peptide is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP 2163. Here, though the claims may recite some functional characteristics, the claims lack written description because there is no disclosure of a correlation between function and structure of the compounds beyond compounds disclosed in the examples in the specification. Moreover, the specification lack sufficient variety of species to reflect this

variance in the genus since the specification does not provide any examples of derivatives. The specification is void of organic molecules that functions as a peptide-like molecule that qualify for the functional characteristics claimed as a peptide or a peptide-like molecule or other peptidic molecules and other synthetic peptide or peptide-like molecule that can form peptide bonds and act as ghrelin like compounds.

16. The specification is limited to the peptide or peptide-like molecules that belong to the same class of protein, ghrelin-like compounds having formula I, Z^1-$(X^1)_m$-(X^2)-$(X^3)_n$-Z^2 and the limitation wherein m is an integer in the range of from 1-10, n is 0 or an integer in the range of from 1-35, and wherein (a) the ghrelin-like compound or pharmaceutically acceptable salt thereof is 27-28 amino acids in length. The specification discloses that "secretagogue" includes the naturally occurring 28 amino acid human ghrelin, the amino acid of which is shown in SEQ ID NO:1, as well as the naturally occurring 27 amino acid human ghrelin, the amino acid of which is shown in SEQ ID NO: 2, and the present invention relates to the use of ghrelin or a peptide homologous thereto (see paragraph [0359]). Furthermore, the reference discloses that the invention includes diastereomers as well as their racemic and resolved enantiomerically pure forms. Secretagogoues can contain, D-amino acids, L-amino acids, alpha-amino acid, beta-amino acid, gamma-amino acid, natural amino acid and synthetic amino acid or the like or a combination thereof. Preferably, amino acids present in a ghrelin-like compound are the L-enantiomer (see paragraph [0360]). The ghrelin-like compound preferably comprises an amino acid modified with a bulky hydrophobic group. The number of amino acids N-terminally to the modified amino acid

is preferably within the range of fro 1-9. Accordingly, m is preferably an integer in the range of from 1-9, 1-8, 1-7, 1-6...1-2 (see paragraph [0360]). The specification further discloses the possible X^1, X^2 and X^3 in the formula I (see paragraphs [0368] to [0375]). The specification further discloses SEQ ID NOS: 1-28 that includes from 1 amino acid (SEQ ID NO: 28) to 28 amino acids (SEQ ID NO:1). The working example describes the Ghrelin (1-9)-NH2, [Ser3(propionyl)]rGhrelin (1-28) synthesis (see Example 2) and using some of these ghrelin-like compound as subcutaneous administration to patients in need thereof (see Examples 6-12). The specification does not describe any other homologous of SEQ ID NO:1, such as derivatives, variants, and other modified amino acids, such as peptidomimetics that form peptide bonds. For example, as describe above, 80% of SEQ ID NO: 1 (28 amino acids) means having at least 23 amino acid homologous to SEQ ID NO:1. Since there are 28 amino acids present in SEQ ID NO:1, this implies that there are 28*6= 168 different possibilities of available homologous. Even at 90% homologous to SEQ ID NO:1, this implies that there are 28*2=56 different homologous possible. Descriptions of SEQ ID NOS:1-28 are not sufficient to encompass numerous other proteins to the same genus. Further, some of the SEQ IDs disclosed do not further limit the broad claim 1. For example, SEQ ID NO:28 consists of amino acid Phe. This is 3% homologous to SEQ ID NO:1, which is not recited in Claim 1. Therefore, description of SEQ ID NOS: 1-28 are not sufficient to encompass numerous other proteins and compounds to the same genus. For example, there are varying lengths, varying amino acid compositions, and numerous distinct qualities that

make up the genus. There is not sufficient amount of examples provided to encompass the numerous characteristics of the whole genus claimed.

17. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate"). Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

2. Claims 1-3, 6, 13-20, 22-23, 27-29, 31, 33-35 and 37 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating cancer cachexia, does not reasonably provide enablement for preventing cancer cachexia. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: (1) the nature or the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the

predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

(1) The nature of the invention:

The invention aims at providing a method for prophylaxis or treatment of cancer cachexia in an individual in need thereof, comprising administering to the subject a secretagogue, such as a ghrelin-like compound for the production of a medicament for the treatment or prevention of cachexia, stimulation of appetite, food intake and/or weight gain, as well as a method of treating or preventing cachexia, stimulating appetite, food intake and/or weight gain in an individual in need thereof by administering a secretagogue, such as a ghrelin-like compound.

(2) The state of the prior art:

The Merck manual indicates that cachexia is wasting of both adipose and skeletal muscle. The condition occurs in many conditions and is common with many cancers when remission or control fails. Merck manual further indicates that in some cancers, especially pancreatic and gastric, cachexia is more profound. Additionally, cachexia is associated with reduced response to chemotherapy, poor functional performance, and increased mortality (see Merck manual, 1st paragraph). Furthermore,

the Merck manual indicates that the primary cause of cachexia is not anorexia or decreased caloric intake. Rather, this complex metabolic condition involves increased tissue catabolism. Protein synthesis is decreased and degradation increased (see Merck manual, 2nd paragraph). The Merck manual indicates that cachexia is easy to recognize, primarily by weight loss, which is most apparent with temporalis muscle mass loss in the face (see Merck manual, 3rd paragraph). Further, the Merck manual indicates that treatment involves treatment of the cancer. If the cancer can be controlled or cured, regardless of modality, cachexia resolves. Additional caloric supplementation does not relieve cachexia, and neither function nor prognosis is improved (see Merck manual 4th and 5th paragraphs). Further, the Merck manual indicates that other treatments can mitigate cachexia and improve function, such as corticosteroids that increase appetite and may improve a sense of well-being, but do little to increase body weight (see Merck manual, 6th paragraph).

Further, Brennan (Cancer Research, 1977, 37: 2359-2364) indicates that host starvation is a common accompaniment to the presence of cancer, and protein conservation are not functioning in the tumor-bearing host (see Summary). The reference indicates that the starvation that accompanies cancer is so well-recognized as to be entitled "cancer cachexia". Further, the reference indicates that determining whether or not the starvation that accompanies cancer is an entity of itself, or simply a manifestation of the malnutrition that accompanies any severe illness is difficult. Patients with gastrointestinal (GI) neoplasms have a clear reason for malnutrition, i.e., inadequate ingestion or digestion of food. In the GI tract, weight loss is often seen as a

reflector of a "hidden" cancer such as cancer of the pancreas. In other small primary lesions not involving the GI tract, such as carcinoma of the lung, weight loss is a similar, almost invariable accompaniment of the presence of cancer (see p. 2359, left column, 1st and 2nd paragraphs). The reference indicates that to examine the problem of cancer cachexia, basic body composition, energy and protein reserves, and the effect of simple starvation on these entities must be reviewed before examining the effect of superimposition of cancer (see p. 2359, left column, 3rd paragraph).

Further, Tisdale MJ (Science, 2000, 289(5488): 2293-2294, herein pp. 1-5) indicates that patients with chronic diseases such as AIDS or cancer (particularly those with tumors of the pancreas, stomach, colon, and lung) often experience a life-threatening muscle wasting syndrome known as cachexia. Although it superficially resembles starvation, it is refractory to nutritional intervention. Loss of skeletal muscle results in lowered mobility, and hence, a poorer quality of life for the patient, and erosion of respiratory muscle eventually leads to death from pneumonia. The reference further indicates that cachexia is associated with reduced survival time irrespective of tumor mass or the presence of metastases, and it also interferes with cancer therapy (see p. 1, 1st column). The reference further indicates the factors involved in activating protein catabolism and blocking cytokine activity for treating cancer cachexia (see p. 2, all). For example, blocking NF-κB activity has been shown to inhibit cachexia in an animal model (see p. 2, last paragraph).

Additionally, Illman (Journal of Support Oncology, 2005, 3(1): 37-50) indicates that cancer-related depression often coincides with uncontrolled appetite loss (anorexia)

and unintentional weight loss (cachexia), especially among those patients whose disease has reached an advanced stage or have a high symptom burden (see p. 37, left column, last paragraph). The reference indicates that increased caloric intake and appetite-inducing drugs have not yet demonstrated an ability to prevent the loss of lean muscle mass in cachectic patients over an extended period, and although useful in treating many of the symptoms of depression in patients with cancer, antidepressants have demonstrated little effect upon the progression of weight loss (see, p. 37, right column, 2nd paragraph). The reference indicates that the effects of cachexia often can be more devastating and debilitating than the growth of the tumor itself (see p. 38, left column, 1st paragraph). Furthermore, the reference indicates that a significant overlap exists between the vegetative symptoms of major depression and cancer-related cachexia, and these symptoms may be related to cytokine activity, patient quality of life, and survival from disease. The release of cytokines induced by the presence of tumor can influence multiple neuroendocrine pathways, altering mood severe enough to cause clinical depression and weight loss; the consequent depression and severe wasting of cachexia are linked to poor compliance with cancer treatments and decreased survival (see p.47, right column, 2nd paragraph). Further, major depression in patients with cancer is treatable with available antidepressant medication; however, to date, cancer-related cachexia is less amenable to treatment (see p. 47, right column, 3rd paragraph).

Thus, the prior arts indicate that cancer cachexia is due to cancer, thus one must have cancer first in order to produce cancer cachexia. The art provide guidance as to

how to treat cancer cachexia, but do not provide guidance as how to how to determine individuals who are susceptible to cancers and thus cancer cachexia.

(3) The relative skill of those in the art:

The relative skill of those in the art is high.

(4) The predictability or unpredictability of the art:

Applicant's activity is based on the determination of predicting those who are susceptible to cancers and cancer cachexia. Since the activity is based on determining the patient population that is susceptible to cancers and cancer cachexia, the predictability in the art is low. This is due to the fact that the art has recognized the difficulty in determining the patient population who are susceptible to cancer.

The Applicant has not shown who will be susceptible cancers and thus, cancer cachexia. There are too many variables between the experimentation, thus, it clearly shows the unpredictability of the art.

(5) The breadth of the claims:

.The claims are drawn to a method for prophylaxis (prevention) or treatment of cancer cachexia in an individual in need thereof, comprising administering a ghrelin-like compound or a pharmaceutically acceptable salt thereof.

(6) The amount of direction or guidance presented and (7) The presence or absence of working examples:

Although the specification provides guidance on how to administer the ghrelin-like compound to patients subcutaneously, it does not provide guidance as when to as when to administer the ghrelin-like compound composition in order to prevent cancer cachexia. The specification discloses the administration of the compound to cancer cachexia patients (see paragraph [0010]). Example 3 shows the safety and dosing experimentation on healthy populations. Example 4 discloses treatment of a patient with established cancer cachexia and reduced appetite, and show after ghrelin-like compound treatment, the patient was able to eat full plates of meals. Example 6 discloses efficacy of subcutaneous administration of ghrelin in mice; Example 7 discloses the efficacy of subcutaneous administration of ghrelin in Gastectomised mice. Example 11 discloses administering ghrelin to cancer cachexia patients in order to improve their food intake and nutritional status over an 8 weeks period. Example 12 discloses experiments to be performed and measured. The specification indicates a prophylaxis and/or alleviation and/or treatment of a clinical depression, which combination treatment further comprises administering an antidepressant, a prodrug, or pharmaceutically acceptable salt thereof (see paragraphs [0579]-[0580]). These experiments are performed on cancerous patients already suffering from cancer and/or cancer cachexia. The specification does not disclose how to prevent cancer, and thus cancer cachexia. Additionally, it is unclear as to when to administer the compound to prevent cancer cachexia. The working examples are directed towards the cancer

patients and those patients suffering from cancer cachexia. As stated above, the specification does not disclose how to prevent cancer, and thus cancer cachexia. The working examples are limited to cancer patients.

As described supra, the Merck manual indicates that cachexia is wasting of both adipose and skeletal muscle. The condition occurs in many conditions and is common with many cancers when remission or control fails. Merck manual further indicates that in some cancers, especially pancreatic and gastric, cachexia is more profound. Additionally, cachexia is associated with reduced response to chemotherapy, poor functional performance, and increased mortality (see Merck manual, 1st paragraph). Furthermore, the Merck manual indicates that the primary cause of cachexia is not anorexia or decreased caloric intake. Rather, this complex metabolic condition involves increased tissue catabolism. Protein synthesis is decreased and degradation increased (see Merck manual, 2nd paragraph). The Merck manual indicates that cachexia is easy to recognize, primarily by weight loss, which is most apparent with temporalis muscle mass loss in the face (see Merck manual, 3rd paragraph). Further, the Merck manual indicates that treatment involves treatment of the cancer. If the cancer can be controlled or cured, regardless of modality, cachexia resolves. Additional caloric supplementation does not relieve cachexia, and neither function nor prognosis is improved (see Merck manual 4th and 5th paragraphs). Further, the Merck manual indicates that other treatments can mitigate cachexia and improve function, such as corticosteroids that increase appetite and may improve a sense of well-being, but do little to increase body weight (see Merck manual, 6th paragraph).

Further, Brennan (Cancer Research, 1977, 37: 2359-2364) indicates that host starvation is a common accompaniment to the presence of cancer, and protein conservation are not functioning in the tumor-bearing host (see Summary). The reference indicates that the starvation that accompanies cancer is so well-recognized as to be entitled "cancer cachexia". Further, the reference indicates that determining whether or not the starvation that accompanies cancer is an entity of itself, or simply a manifestation of the malnutrition that accompanies any severe illness is difficult. Patients with gastrointestinal (GI) neoplasms have a clear reason for malnutrition, i.e., inadequate ingestion or digestion of food. In the GI tract, weight loss is often seen as a reflector of a "hidden" cancer such as cancer of the pancreas. In other small primary lesions not involving the GI tract, such as carcinoma of the lung, weight loss is a similar, almost invariable accompaniment of the presence of cancer (see p. 2359, left column, 1st and 2nd paragraphs). The reference indicates that to examine the problem of cancer cachexia, basic body composition, energy and protein reserves, and the effect of simple starvation on these entities must be reviewed before examining the effect of superimposition of cancer (see p. 2359, left column, 3rd paragraph).

Further, Tisdale MJ (Science, 2000, 289(5488): 2293-2294, herein pp. 1-5) indicates that patients with chronic diseases such as AIDS or cancer (particularly those with tumors of the pancreas, stomach, colon, and lung) often experience a life-threatening muscle wasting syndrome known as cachexia. Although it superficially resembles starvation, it is refractory to nutritional intervention. Loss of skeletal muscle results in lowered mobility, and hence, a poorer quality of life for the patient, and erosion

of respiratory muscle eventually leads to death from pneumonia. The reference further indicates that cachexia is associated with reduced survival time irrespective of tumor mass or the presence of metastases, and it also interferes with cancer therapy (see p. 1, 1st column). The reference further indicates the factors involved in activating protein catabolism and blocking cytokine activity for treating cancer cachexia (see p. 2, all). For example, blocking NF-κB activity has been shown to inhibit cachexia in an animal model (see p. 2, last paragraph).

Additionally, Illman (Journal of Support Oncology, 2005, 3(1): 37-50) indicates that cancer-related depression often coincides with uncontrolled appetite loss (anorexia) and unintentional weight loss (cachexia), especially among those patients whose disease has reached an advanced stage or have a high symptom burden (see p. 37, left column, last paragraph). The reference indicates that increased caloric intake and appetite-inducing drugs have not yet demonstrated an ability to prevent the loss of lean muscle mass in cachectic patients over an extended period, and although useful in treating many of the symptoms of depression in patients with cancer, antidepressants have demonstrated little effect upon the progression of weight loss (see, p. 37, right column, 2nd paragraph). The reference indicates that the effects of cachexia often can be more devastating and debilitating than the growth of the tumor itself (see p. 38, left column, 1st paragraph). Furthermore, the reference indicates that a significant overlap exists between the vegetative symptoms of major depression and cancer-related cachexia, and these symptoms may be related to cytokine activity, patient quality of life, and survival from disease. The release of cytokines induced by the presence of tumor

can influence multiple neuroendocrine pathways, altering mood severe enough to cause clinical depression and weight loss; the consequent depression and severe wasting of cachexia are linked to poor compliance with cancer treatments and decreased survival (see p.47, right column, 2nd paragraph). Further, major depression in patients with cancer is treatable with available antidepressant medication; however, to date, cancer-related cachexia is less amenable to treatment (see p. 47, right column, 3rd paragraph).

Thus, the prior arts indicate that cancer cachexia is due to cancer, thus one must have cancer first in order to produce cancer cachexia. The art provide guidance as to how to treat cancer cachexia, but do not provide guidance as how to how to determine individuals who are susceptible to cancers and thus cancer cachexia.

The specification has not provided guidance in the way of a disclosure to how to determine individuals that need protection against cancers, and thus cancer cachexia. There is no clear guidance as to how to determine the patient population, since cancer is an unregulated proliferation of cells due to loss of normal controls, resulting in unregulated growth, lack of differentiation, local tissue invasion, and often, metastasis. Cancer can develop in any tissue or organ at any age, and it is unclear who would develop cancers, and thus cancer cachexia, more guidance is necessary. Further, as indicated above, cancer cachexia can also be due to depression of cancer patients. Increasing appetite would not enhance the appetite in those suffering from depression (emotional and psychological problems leading to appetite loss and weight loss). Since the prior art is still unclear as to who are susceptible to cancers, more guidance is necessary.

(8) The quantity of experimentation necessary:

Since it is uncertain to predict the patient population who are susceptible for cancers, and the Applicant have not provided the appropriate time frame at which the compound should be administered, one of ordinary skill in the art would be burdened with undue "painstaking experimentation study" to determine if the ghrelin-like compounds would be effective in preventing cancers and cancer cachexia.

Please note that the term "prevent" as well as "prophylaxis" in an absolute definition which means to stop from occurring and, thus, requires a higher standard for enablement than does "therapeutic" or "treat" or "alleviate", especially since it is notoriously well accepted in the medical art that the vast majority of afflictions/disorders suffered by mankind cannot be totally prevented with current therapies (other than certain vaccination regimes)- including preventing such disorders as cancers and cancer cachexia, which is clearly not recognized in the medical art as being totally preventable condition.

Rejection-35 U.S.C. 102

19. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

20. Claims 1-3, 6, 13-18, 20, 22, 27-29, 31, 33-35, 39-40 and 43-44 are rejected under 35 U.S.C. 102(b) as being anticipated by Bednarek MA (WO 01/92292 A2).

21. The instant claims are drawn to a method for prophylaxis or treatment of cancer cachexia in an individual in need thereof, comprising administration to the individual of a ghrelin-like compound or a pharmaceutically acceptable salt thereof, wherein the ghrelin-like compound comprises a structure defined by formula I, and wherein (a) said ghrelin-like compound or pharmaceutically acceptable salt thereof is 27-28 amino acids in lengths, with the proviso that said ghrelin-like compound is at least 80% homologous to SEQ ID NO:1.

22. Bednarek MA patent teaches truncated ghrelin analogs active at the GHS receptor and these analogs have a variety of different uses including being used as a research tool and being used therapeutically (see abstract). The reference further teaches SEQ ID NO:1 (the structure of human ghrelin with modified serines), and teaches that the core region at position 2 or 3 is modified with a bulky hydrophobic R group (p.3, lines 11-20). This meets the limitation of claims 1-3, 6, 13-14 and 39-40, since SEQ ID NO:1 of the reference is the same as the SEQ ID NO: 1 of instant claims, thus meeting the limitation of at least 80% sequence homology to SEQ ID NO:1. The reference further teaches a truncated ghrelin analog having a structure selected from the group consisting of Z^1-GSXF$(Z)_n$-Z^2 or Z^1-GXSF$(Z)_n$-Z^2, wherein Z1 is optionally present protecting group , Z2 is an optionally present protecting group, n is 0 to 19 or a pharmaceutically acceptable salt thereof (see p. 3, lines 21-32 and p. 4, lines 1-4) and teaches SEQ ID NO: 4 (p. 27, line 16) which is at least 80% of SEQ ID NO: 1 (i.e., 23

amino acids in lengths). This meets the limitation of claims 1-2, 6 and 39. Furthermore, the reference teaches that ghrelin agonists can be used to achieve a beneficial effect in a subject (mammals, including a human, rat, a mouse, or a farm animal) such as one or more of the following: treating growth hormone deficient state, increasing muscle mass...facilitating weight gain, facilitating maintenance of weight, facilitation maintenance of physical function...facilitating appetite increase. Facilitating a weight gain, maintenance in weight, or appetite increase is particularly useful for a patient having a disease or disorder, or undergoing a treatment, accompanied by weight loss...anorexia, bulimia, cancer cachexia, AIDS, wasting, cachexia, and wasting in frail elderly. Examples of treatments accompanied by weight loss include chemotherapy, radiation therapy, temporary or permanent immobilization, and dialysis (see p. 5, lines 23-35 and p. 6, lines 1-6). This reads on claims 27-29, 31, 33-35, 39-40 and 44, since lipodystrophy (loss of fat from one area due to multiple injections at the same site) can be a possible side effect of antiretroviral drugs. Furthermore, the Applicant has pointed out that the treatment is directed to cancer cachexia, a condition not dependent on cancer type (see Applicant's election with traverse, p. 4). Furthermore, since the reference discloses that the treatments accompanied by weight loss include chemotherapy, radiation therapy, and since cancer is being treated along with cancer cachexia, this reads on claims 33-35. The reference further teaches that the ghrelin analog can be administered by nasal aerosol or inhalation formulations may be prepared, for example, as solutions in saline, and in intravenous (both bolus and infusion), intraperitoneal, subcutaneous, topical with or without occlusion, or

intramuscularly. When administered by injection, the injectable solution or suspension may be formulated using suitable non-toxic, parenterally acceptable diluents or solvents, such as Ringer's solution or isotonic sodium chloride solution, or suitable dispersion or wetting and suspending agents, such as sterile, bland, fixed oils, including synthetic mono- or diglycerides, and fatty acids, including oleic acid (see p. 15, lines 9-20). This reads on claims 15-18. Furthermore, the reference teaches that truncated ghrelin analogs can be provided in a kit, such a kit typically contains an active compound in dosage forms for administration (see p. 15, lines 30-31). This further reads on claim 16, since the reference teaches that an injectable solution or suspension may be formulated using suitable non-toxic solvents. The reference further teaches that the daily dose for a subject is expected to be between 0.01 mg (10 μg) and 1000 mg per subject per day (see p. 15, lines 28-29). This reads on claims 20, 22 and 43. Please note that the reference teaches that the core region at position 2 or 3 is modified with a bulky hydrophobic R group (p.3, lines 11-20), which is claimed in claim 5 of instant application. This claim is withdrawn from consideration, as being drawn to a nonelected species, SEQ ID NO: 1, which comprises modification at position 3.

Rejection-35 U.S.C. 103

23. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

24. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

25. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

26. Claim 37 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bednarek MA (WO 01/92292 A2) as applied to claims1-3, 6, 13-18, 20, 22, 27-29, 31, 33-35, 39-40 and 43-44 above, and further in view of Okamoto T (International Journal of Molecular Medicine, 2002, 9: 369-372).

27. The instant claims are drawn to a method for prophylaxis or treatment of cancer cachexia in an individual in need thereof, comprising administration to the individual of a ghrelin-like compound or a pharmaceutically acceptable salt thereof, wherein the ghrelin-like compound comprises a structure defined by formula I, and wherein (a) said

ghrelin-like compound or pharmaceutically acceptable salt thereof is 27-28 amino acids in lengths, with the proviso that said ghrelin-like compound is at least 80% homologous to SEQ ID NO:1. The claims are further drawn to the method further comprising administration of an effective amount of an NSAID medicament.

28. The teachings of Bednarek are described supra. The difference between the reference and the instant claims is that the reference does not teach further administration of NSAID medicament for treating cancer cachexia.

29. However, Okamoto T teaches that zaltoprogen (a non-steroidal anti-inflammatory drug) causes potent inhibition of cyclooxygenase-2 with fewer side effects on the gastrointestinal tract. Zaltoprofen improves the loss in body weight in both Con A-treated mice and carbon tetrachloride-treated rats. These results suggest the possible application of zaltoprogen for the treatment of sickness behaviors including loss of body weight occurring in cancer cachexia (see abstract, p. 370, left and right columns and conclusion, pp. 370-371). The reference further discloses that administration of aspirin or indomethacin prolongs the survival of patients with esophageal cancer, stomach cancer, and rectal cancer. The mechanism underlying the ability of NSAIDs to prolong the survival of cancer patients is not known, but the present results with zaltoprofen improves the body weight loss in rodent sickness behavior model, suggest protection against wasting (see p. 371, right column, 1st paragraph).

30. Therefore, it would have been obvious to one of ordinary skill in the art to combine the teachings of Bednarek and Okamoto since both prior arts teach treating cancer cachexia. There is a reasonable expectation of success, since zaltoprofen

protects against wasting in cancer and behavior sickness models and ghrelin analogs are effective in facilitating a weight gain, maintenance in weight or appetite increase in patients having a disease or disorder. Furthermore, the MPEP states the following: "It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980) (citations omitted) (Claims to a process of preparing a spray-dried detergent by mixing together two conventional spray-dried detergents were held to be prima facie obvious.). See also *In re Crockett*, 279 F.2d 274, 126 USPQ 186 (CCPA 1960) (Claims directed to a method and material for treating cast iron using a mixture comprising calcium carbide and magnesium oxide were held unpatentable over prior art disclosures that the aforementioned components individually promote the formation of a nodular structure in cast iron.); and *Ex parte Quadranti*, 25 USPQ2d 1071 (Bd. Pat. App. & Inter. 1992) (mixture of two known herbicides held prima facie obvious). But see *In re Geiger*, 815 F.2d 686, 2 USPQ2d 1276 (Fed. Cir. 1987) ("Based upon the prior art and the fact that each of the three components of the composition used in the claimed method is conventionally employed in the art for treating cooling water systems, the board held that it would have been prima facie obvious, within the meaning of 35 U.S.C. 103, to employ these components in combination for their known functions and to optimize the amount of each additive....Appellant argues... hindsight reconstruction or at best,... obvious to try'.... We

agree with appellant."). Since Bednarek teaches using ghrelin analog to treat cancer cachexia and Okamoto teaches using NSAID to treat cancer cachexia, there is a reasonable expectation of success, since combining the two compounds would at least have an additive effect.

31. Claims 19 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bednarek MA (WO 01/92292 A2) as applied to claims1-3, 6, 13-18, 20, 22, 27-29, 31, 33-35, 39-40 and 43-44 above.

32. The instant claims are drawn to a method for prophylaxis or treatment of cancer cachexia in an individual in need thereof, comprising administration to the individual of a ghrelin-like compound or a pharmaceutically acceptable salt thereof, wherein the ghrelin-like compound comprises a structure defined by formula I, and wherein (a) said ghrelin-like compound or pharmaceutically acceptable salt thereof is 27-28 amino acids in lengths, with the proviso that said ghrelin-like compound is at least 80% homologous to SEQ ID NO:1. The claims are further drawn to the method wherein the medicament is administered prior to or during a meal and the method wherein the medicament is administered as a bolus prior to or during a meal, said bolus comprising an amount of ghrelin-like compound of a salt thereof equivalent to from 0.3 μg to 600 mg ghrelin.

33. The teachings of Bednarek are described supra. The difference between the reference and the instant claims is that the reference does not teach when the medicament is administered.

34. However, it would have been obvious to one of ordinary skill in the art to try different time points of administering the medicament. It has been held that under KSR that "obvious to try" may be an appropriate test under 103. The Supreme Court stated in KSR, When there is motivation "to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under § 103." *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727,_,82 USPQ2d 1385, 1397 (2007).

35. The "problem" facing those in the art was when to administer the medicament to achieve the optimal conditions for the treatment of cancer cachexia (facilitate weight gain, maintenance of weight, facilitate appetite increase, etc), and there were a limited number of methodologies available to do so, for example Bednarek discloses that daily dose for a subject is expected to be between 0.01 mg (10 μg) and 1000 mg per subject per day and a desirable effect can be obtained when administered to a subject during regular intervals, such as 1 to 6 times a day, during the course of 1 or more days, and the kit contains instructions indicating the use of the dosage form to achieve a desirable affect and the amount of dosage form to be taken over a specified time period (see pp. 15-16, WO 01/92292 A2). The skilled artisan would have had reason to try different time points and before, after and during a meal of administration of the medication methodologies with the reasonable expectation that at least one would be successful.

Since the ghrelin analogs can be used to facilitate a weight gain, maintain weight and facilitate appetite increase in patients suffering from bulimia, cancer cachexia, AIDS, wasting cachexia and wasting in frail elderly, thus, administering ghrelin analogs prior to meal or during a meal for treating cancer cachexia in the dosage claimed is a "the product not of innovation but of ordinary skill and common sense," leading to the conclusion that invention is not patentable as it would have been obvious.

Conclusion

36. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Julie Ha whose telephone number is 571-272-5982. The examiner can normally be reached on Mon-Fri, 8:00 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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